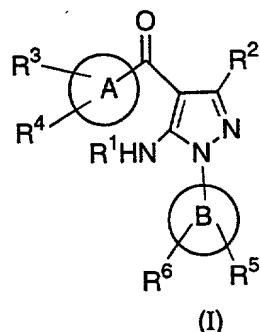


What is Claimed:

1. A compound selected from the group of compounds represented by Formula (I):



(I)

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wherein:

R¹ is hydrogen or acyl;

R² is hydrogen or alkyl;

A is an aryl or heteroaryl ring;

B is an aryl or heteroaryl ring;

R³ is selected from the group consisting of:

- (a) amino, alkylamino or dialkylamino;
- (b) acylamino;
- (c) optionally substituted heterocyclil;
- (d) optionally substituted aryl or heteroaryl;
- (e) heteroalkyl;
- (f) heteroalkenyl;
- (g) heteroalkynyl;
- (h) heteroalkoxy;
- (i) heteroalkylamino;
- (j) optionally substituted heterocyclalkyl;
- (k) optionally substituted heterocyclalkenyl;
- (l) optionally substituted heterocyclalkynyl;
- (m) optionally substituted heterocyclalkoxy, cycloxy or heterocyclyoxy;

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- (n) optionally substituted heterocyclalkylamino;
- (o) optionally substituted heterocyclalkylcarbonyl;
- (p) heteroalkylcarbonyl;
- (q) -NHSO₂R⁶ where R⁶ is alkyl, heteroalkyl or optionally substituted heterocyclalkyl;
- (r) -NHSO₂NR⁷R⁸ where R⁷ and R⁸ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (s) -Y-(alkylene)-R⁹ where:
 - Y is a single bond, -O-, -NH- or -S(O)_n- (where n is an integer from 0 to 2); and
 - R⁹ is cyano, optionally substituted heteroaryl, -COOH, -COR¹⁰, -COOR¹¹, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹, where R¹⁰ is alkyl or optionally substituted heterocycle, R¹¹ is alkyl, and R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (t) -C(=NR²⁰)(NR²¹R²²) where R²⁰, R²¹ and R²² independently represent hydrogen, alkyl or hydroxy, or R²⁰ and R²¹ together are -(CH₂)_n- where n is 2 or 3 and R²² is hydrogen or alkyl;
- (u) -NHC(X)NR²³R²⁴ where X is -O- or -S-, and R²³ and R²⁴ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (v) -CONR²⁵R²⁶ where R²⁵ and R²⁶ independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or R²⁵ and R²⁶ together with the nitrogen to which they are attached form an optionally substituted heterocycl ring;
- (w) -S(O)_nR²⁷ where n is an integer from 0 to 2, and R²⁷ is alkyl, heteroalkyl, optionally substituted heterocyclalkyl or

-NR²⁸R²⁹ where R²⁸ and R²⁹ are, independently of each other,
hydrogen, alkyl or heteroalkyl;

(x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all
optionally substituted with alkyl, halo, hydroxy or amino;

5 (y) arylaminoalkylene or heteroaryl aminoalkylene;

(z) Z-alkylene-NR³⁰R³¹ or Z-alkylene-OR³² where Z is -NH-, -
N(lower alkyl)- or -O-, and R³⁰, R³¹ and R³² are independently of
each other, hydrogen, alkyl or heteroalkyl;

10 (aa) -OC(O)-alkylene-CO₂H or -OC(O)-NR'R'' (where R' and R''
are independently hydrogen or alkyl); and

(bb) heteroarylalkenylene or heteroarylalkynylene;

R⁴ is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) alkoxy; and

(e) hydroxy;

R⁵ is selected from the group consisting of :

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) haloalkyl;

(e) thioalkyl;

(f) hydroxy;

20 (g) amino;

(h) alkylamino;

(i) dialkylamino;

(j) heteroalkyl;

(k) optionally substituted heterocycle;

25 (l) optionally substituted heterocyclalkyl;

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- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or di-alkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from the group consisting of:

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- (a) hydrogen;
- (b) halo;
- (c) alkyl; and
- (d) alkoxy;

15 prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

20 2. The compound of Claim 1 wherein R³ is:

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- (a) optionally substituted heterocyclyl;
- (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO₂R' (where R' is alkyl) or SO₂NHR'R" (where R' and R" are independently hydrogen or alkyl);
- (c) heteroalkyl;
- (d) heteroalkenyl;
- (e) heteroalkylamino;
- (f) heteroalkoxy;
- (g) optionally substituted heterocyclalkyl or heterocyclyloxy;
- (h) optionally substituted heterocyclalkenyl;
- (i) optionally substituted heterocyclalkynyl;
- (j) optionally substituted heterocyclalkoxy;
- (k) optionally substituted heterocyclalkylamino;
- (l) optionally substituted heterocyclalkylcarbonyl;

(k) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶ -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;

5 (l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(m) arylaminoalkylene or heteroarylaminoalkylene; or

(n) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

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3. The compound of Claim 2 wherein R¹ and R² are hydrogen; and B is phenyl.

4. The compound of Claim 3 wherein A is phenyl.

15 5. The compound of Claim 4 wherein R⁴ is hydrogen; and R⁵ is halo or alkyl.

6. The compound of Claim 5 wherein R⁵ is chloro, fluoro or methyl; and R⁶ is hydrogen, chloro, fluoro, methyl or methoxy.

20 7. The compound of Claim 5, wherein R³ is optionally substituted heteroaryl.

8. The compound of Claim 7, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.

25 9. The compound of Claim 8, wherein R³ is at the 3-position.

10. The compound of Claim 9, wherein R⁵ is 4-F and R⁶ is hydrogen.

30 11. The compound of Claim 9, wherein R⁵ is 2-Me and R⁶ is hydrogen.

12. The compound of Claim 5, wherein R³ is optionally substituted phenyl.

13. The compound of Claim 12, wherein R³ is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

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14. The compound of Claim 13, wherein R³ is at the 3-position.

15. The compound of Claim 14, wherein R⁵ is 4-F and R⁶ is hydrogen.

10 16. The compound of Claim 5, wherein R³ is:

- (a) heteroalkyl;
- (b) heteroalkoxy;
- (c) heteroalkylamino;
- (d) optionally substituted heterocyclalkyl;
- (e) optionally substituted heterocyclalkoxy;
- (f) optionally substituted heterocyclalkylamino;
- (g) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶ - NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶ R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl; or
- (h) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

20 25 17. The compound of Claim 16, wherein R³ is heteroalkyl.

18. The compound of Claim 17, wherein R³ is at the 3-position and is selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, 2-dimethylaminoethylamino, 3-dimethylaminopropylamino, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-hydroxybutyl.

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19. The compound of Claim 18, wherein R⁵ is 2-F and R⁶ is 4-F.

20. The compound of Claim 18, wherein R⁵ is 4-F and R⁶ is hydrogen.

5 21. The compound of Claim 18, wherein R⁵ is 2-Me and R⁶ is hydrogen.

22. The compound of Claim 16, wherein R³ is heteroalkoxy or heteroalkylamino.

10 23. The compound of Claim 22, wherein R³ is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.

24. The compound of Claim 23 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.

15 25. The compound of Claim 16, wherein R³ is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.

20 26. The compound of Claim 25, wherein R³ is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxypiperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

27. The compound of Claim 26 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.

28. The compound of Claim 16 wherein R³ is -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶ -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl.

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29. The compound of Claim 28, wherein Y is a single bond and R⁹ is SO₂R¹⁴ or -SO₂NR¹⁵R¹⁶.

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30. The compound of Claim 29 wherein R³ is methylsulfonyleethyl or sulfamoyleethyl.

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31. The compound of Claim 30 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.

32. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable excipient.

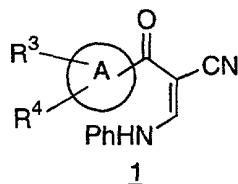
33. A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound of Claim 1.

20 34. The method of Claim 33 wherein the disease is an inflammatory disease.

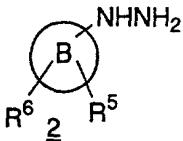
35. The method of Claim 34 wherein the disease is arthritis.

36. A process for preparing a compound of Formula (I) selected from compounds of Claim 1, which process comprises:

25 (i) reacting a 2-keto-3-phenylaminoacrylonitrile of Formula 1:



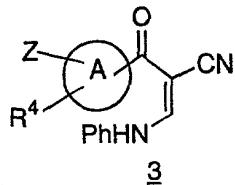
with a hydrazine of Formula 2:



where R^3 , R^4 , R^5 and R^6 are as defined in Claim 1 to provide a compound of Formula

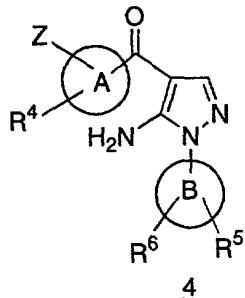
(I) where R^1 is hydrogen; or

(ii) reacting a 2-keto-3-phenylaminoacrylonitrile of formula 3:



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where Z is either hydroxy, nitro or halo group and R^4 are as defined in Claim 1 with a hydrazine of formula 2 to provide a compound of formula 4:

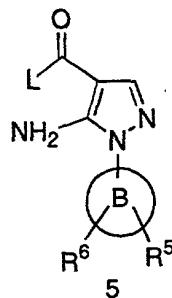


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followed by conversion of the Z group to the desired R^3 group to provide a compound of Formula (I) where R^1 is hydrogen;

- (iii) optionally modifying any of the R^1 , R^3 , R^4 , R^5 or R^6 groups;
- (iv) optionally converting the compound of Formula (I) prepared in Steps (i), (ii) or (iii) above, to the corresponding acid addition salt by treatment with an acid;
- (v) optionally converting the compound of Formula (I) prepared in Steps (i), (ii) or (iii) above, to the corresponding free base by treatment with a base; and
- (vi) optionally separating a mixture of stereoisomers of a compound of Formula (I) prepared in Steps (i) - (v) above, to give a single stereoisomer.

37. A process for preparing a compound of Formula (I) selected from compounds of Claim 1, which process comprises reacting a compound of Formula 5:



where L is a leaving group under organometallic displacement reaction conditions

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with an organometallic reagent of formula R^4-A-M^+ where M is a metallic moiety to provide a compound of Formula (I) where R¹ is hydrogen;

(ii) optionally modifying any of the R¹, R³, R⁴, R⁵ or R⁶ groups;

(iii) optionally converting the compound of Formula (I) prepared in Steps (i) or (ii) above, to the corresponding acid addition salt by treatment with an acid;

(iv) optionally converting the compound of Formula (I) prepared in Steps (i) or (ii) above, to the corresponding free base by treatment with a base; and

15 (v) optionally separating a mixture of stereoisomers of a compound of Formula (I) prepared in Steps (i) or (iv) above, to give a single stereoisomer.

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